

Figure 1

Heteractis crispa chromoprotein wild type (base isoform)

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      10      20      30      40      50      60
5' ACCATTTGCTTTGGTTCCTTGGCAAACGAAAGTTTAGAACGAAAAGTATGACCCAAATTACA
      70      80      90     100     110     120
TCTTCCTCCTGGATCCTTACCATGGCTGGTTTGTGAAAGAAAGTATGCGCATCAAGATG
      M A G L L K E S M R I K M
     130     140     150     160     170     180
TACATGGAAGGCACGGTTAATGGCCATTATTTCAAGTGTGAAGGAGAGGGAGACGGCAAC
Y M E G T V N G H Y F K C E G E G D G N
     190     200     210     220     230     240
CCATTTACAGGTACGCAGAGCATGAGGATTCATGTCACCGAAGGGGCTCCATTACCATTT
P F T G T Q S M R I H V T E G A P L P F
     250     260     270     280     290     300
GCCTTCGACATTTTGGCACCGTGTGTGAGTACGGCAGCAGGACCTTTGTCCACCATACG
A F D I L A P C C E Y G S R T F V H H T
     310     320     330     340     350     360
GCAGAGATTCCCGATTTCTTCAAGCAGTCTTTCCCTGAAGGCTTTACTTGGGAAAGAACC
A E I P D F F K Q S F P E G F T W E R T
     370     380     390     400     410     420
ACAACCTATGAAGATGGAGGCATTCTTACTGCTCATCAGGACACAAGCCTGGAGGGGAAC
T T Y E D G G I L T A H Q D T S L E G N
     430     440     450     460     470     480
TGCCTTATATACAAGGTGAAAGTCCTTGGTACCAATTTTCCTGCTGATGGCCCCGTGATG
C L I Y K V K V L G T N F P A D G P V M
     490     500     510     520     530     540
AAGAACAAATCAGGAGGATGGGAGCCATGCACTGAGGTGGTTTATCCAGAGAATGGTGTC
K N K S G G W E P C T E V V Y P E N G V
     550     560     570     580     590     600
CTGTGTGGACGTAATGTGATGGCCCTTAAAGTCGGTGATCGTCGTTTGATCTGCCATCTC
L C G R N V M A L K V G D R R L I C H L
     610     620     630     640     650     660
TATACTTCTTACAGGTCCAAGAAAGCAGTCCGTGCCTTGACAATGCCAGGATTTTCATTTT
Y T S Y R S K K A V R A L T M P G F H F
     670     680     690     700     710     720
ACAGACATCCGCCTTCAGATGCCGAGGAAAAAGAAAGACGAGTACTTTGAACTGTACGAA
T D I R L Q M P R K K K D E Y F E L Y E
     730     740     750     760     770     780
GCATCTGTGGCTAGGTACAGTGATCTTCCTGAAAAAGCAAATTGATTGTTCCCAGTGACA
A S V A R Y S D L P E K A N *
     790     800     810     820     830     840
CCAGACTGCTGTCAGCTTTTGGTTAAAGCCCGAAAGACAAAAGGACATTTGTAGTTTAGT
     850     860     870     880     890     900
TTATATTTCCCTTTTCATTTGTGAATCAACATTGTACTCTCTGTAAACCTTTAAAATGCTC
     910
CATTAACCT 3' (SEQ ID NOS: 01 & 02)

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DDBJ/EMBL/GenBank

Figure 2

Heteractis crispa chromoprotein wild type (second isoform)

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      10      20      30      40      50      60
5' ACCATTTGCTTTGGTTCCTTGGCAAACGAAAGTTTAGACGAAAACTGACCCAAATTACAT

      70      80      90     100     110     120
CCTCCTGATCCTTACCATGGCTGGTTTGGTTGAAAGAAAGTATGCGCATCAAGATGTACAT
      M A G L L K E S M R I K M Y M

     130     140     150     160     170     180
GGAAGGCACGGTTAATGGCCATTATTTCAAGTGTGAAGGAGAGGGAGACGGCAACCCATT
      E G T V N G H Y F K C E G E G D G N P F

     190     200     210     220     230     240
TACAGGTACGCAGAGCATGAGGATTCATGTCACCGAAGGGGCTCCATTACCATTTCGCTT
      T G T Q S M R I H V T E G A P L P F A F

     250     260     270     280     290     300
CGACATTTTGGCACCGTGTGTGAGTACGGCAGCAGGACCTTTGTCCACCATACGGCAGA
      D I L A P C C E Y G S R T F V H H T A E

     310     320     330     340     350     360
GATTCCCGATTTCTTCAAGCAGTCTTTCCTGAAGGCTTTACTTGGGAAAGAACCACAAC
      I P D F F K Q S F P E G F T W E R T T T

     370     380     390     400     410     420
CTATGAAGATGGAGGCATTCTTACTGCTCATCAGGACACAAGCCTGGAGGGGAACTGCCT
      Y E D G G I L T A H Q D T S L E G N C L

     430     440     450     460     470     480
TATATACAAGGTGAAAGTCCTTGGTACCAATTTTCCTGCTGATGGCCCCGTGATGAAGAA
      I Y K V K V L G T N F P A D G P V M K N

     490     500     510     520     530     540
CAAATCAGAAGGATGGGAGCCATGCACTGAGGTGGTTTATCCAGATAATGGTGTCTGTG
      K S E G W E P C T E V V Y P D N G V L C

     550     560     570     580     590     600
TGGACGTAATGTGATGGCCCTTAAAGTCGGTGATCGTCGTTTGATCTGCCATCTCTATAC
      G R N V M A L K V G D R R L I C H L Y T

     610     620     630     640     650     660
TTCTTACAGGTCCAAGAAAGCAGTCCGTGCCTTGACAATGCCAGGATTTTCATTTTACAGA
      S Y R S K K A V R A L T M P G F H F T D

     670     680     690     700     710     720
CATCCGCCTTCAGATGCCGAGGAAAAAGAAAGACGAGTACTTTGAACTGTACGAAGCATC
      I R L Q M P R K K K D E Y F E L Y E A S

     730     740     750     760     770     780
TGTGGCTAGGTACAGTGATCTTCCTGAAAAAGCAAATTGATTGTTCCAGTGACACCAGA
      V A R Y S D L P E K A N *

     790     800     810     820     830     840
CTGCTGTCAGCTTTTGGTTAAAGCCCGAAAGACAAAAGGACATTTGTAGTTTTAGTTTAT

     850     860     870     880     890     900
ATTTTCCCTTTCATTTTGTGAATCAACATTGTACTCTCTGTAAACCTTTAAATGCTCCA

TTAAACCT 3' (SEQ ID NOS: 03 & 04)
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Figure 3

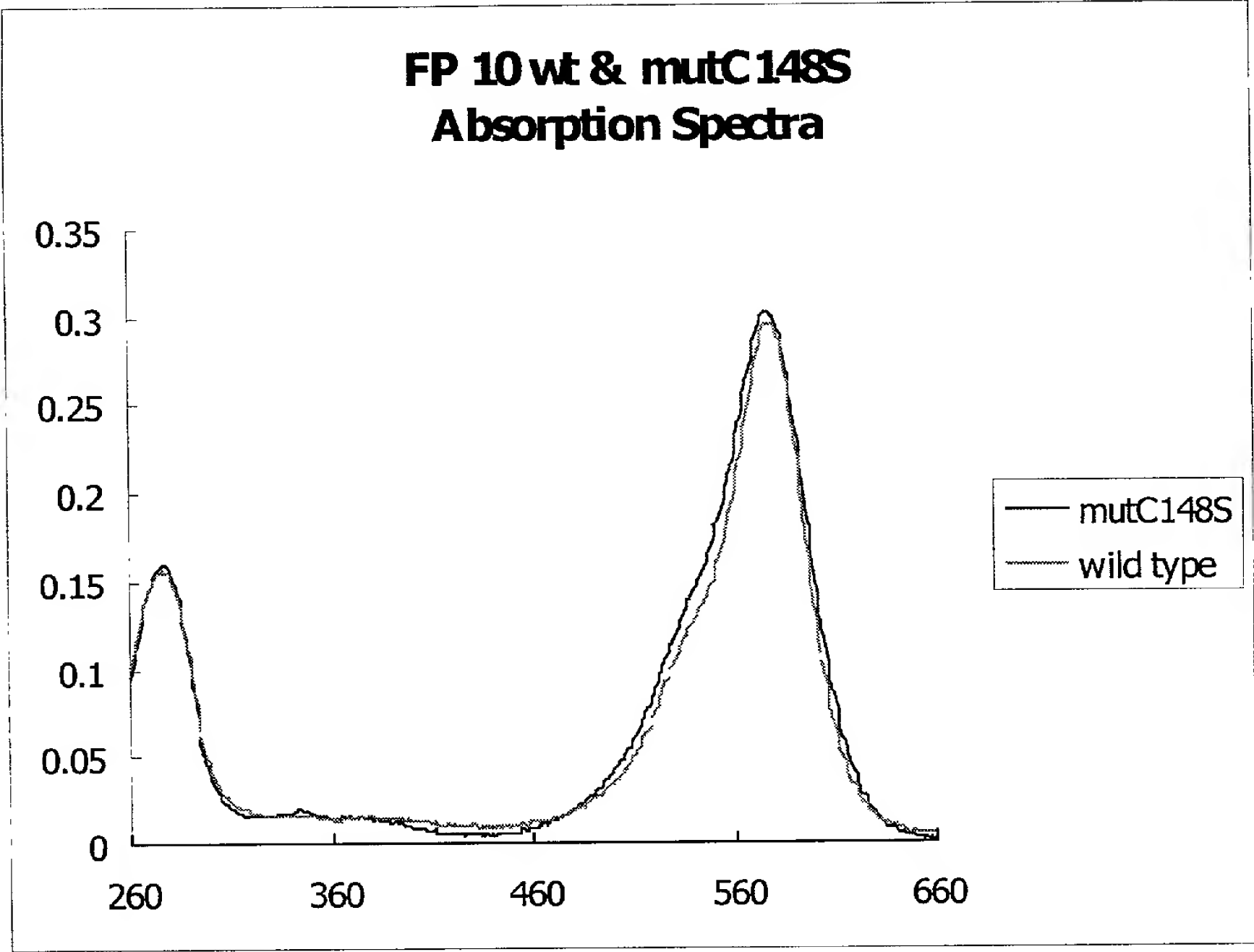


Figure 4

Heteractis crispa fluorescent protein **mutant C148S**

C148S according to GFP numbering

C143S according to self-numbering.

ATGGCTGGTTTGTGAAAGAAAGTATGCGCATCAAGATG
M A G L L K E S M R I K M

TACATGGAAGGCACGGTTAATGGCCATTATTTCAAGTGTGAAGGAGAGGGAGACGGCAAC
Y M E G T V N G H Y F K C E G E G D G N

CCATTTACAGGTACGCAGAGCATGAGGATTCATGTCACCGAAGGGGCTCCATTACCATTT
P F T G T Q S M R I H V T E G A P L P F

GCCTTCGACATTTTGGCACCGTGTGAGTACGGCAGCAGGACCTTTGTCCACCATACG
A F D I L A P C C E Y G S R T F V H H T

GCAGAGATTCCCGATTTCTTCAAGCAGTCTTCCCTGAAGGCTTTACTTGGGAAAGAACC
A E I P D F F K Q S F P E G F T W E R T

ACAACCTATGAAGATGGAGGCATTCTTACTGCTCATCAGGACACAAGCCTGGAGGGGAAC
T T Y E D G G I L T A H Q D T S L E G N

TGCCTTATATACAAGGTGAAAGTCCTTGGTACCAATTTTCCTGCTGATGGCCCCGTGATG
C L I Y K V K V L G T N F P A D G P V M

AAGAACAAATCAGGAGGATGGGAGCCAAGCACTGAGGTGGTTTATCCAGAGAATGGTGTG
K N K S G G W E P S T E V V Y P E N G V

CTGTGTGGACGTAATGTGATGGCCCTTAAAGTCGGTGATCGTCGTTTGATCTGCCATCTC
L C G R N V M A L K V G D R R L I C H L

TATACTTCTTACAGGTCCAAGAAAGCAGTCCGTGCCTTGACAATGCCAGGATTTTCATTTT
Y T S Y R S K K A V R A L T M P G F H F

ACAGACATCCGCCTTCAGATGCCGAGGAAAAAGAAAGACGAGTACTTTGAACTGTACGAA
T D I R L Q M P R K K K D E Y F E L Y E

GCATCTGTGGCTAGGTACAGTGATCTTCCTGAAAAAGCAAATTGA
A S V A R Y S D L P E K A N *

(SEQ ID NOS: 05 & 06)

Figure 5A

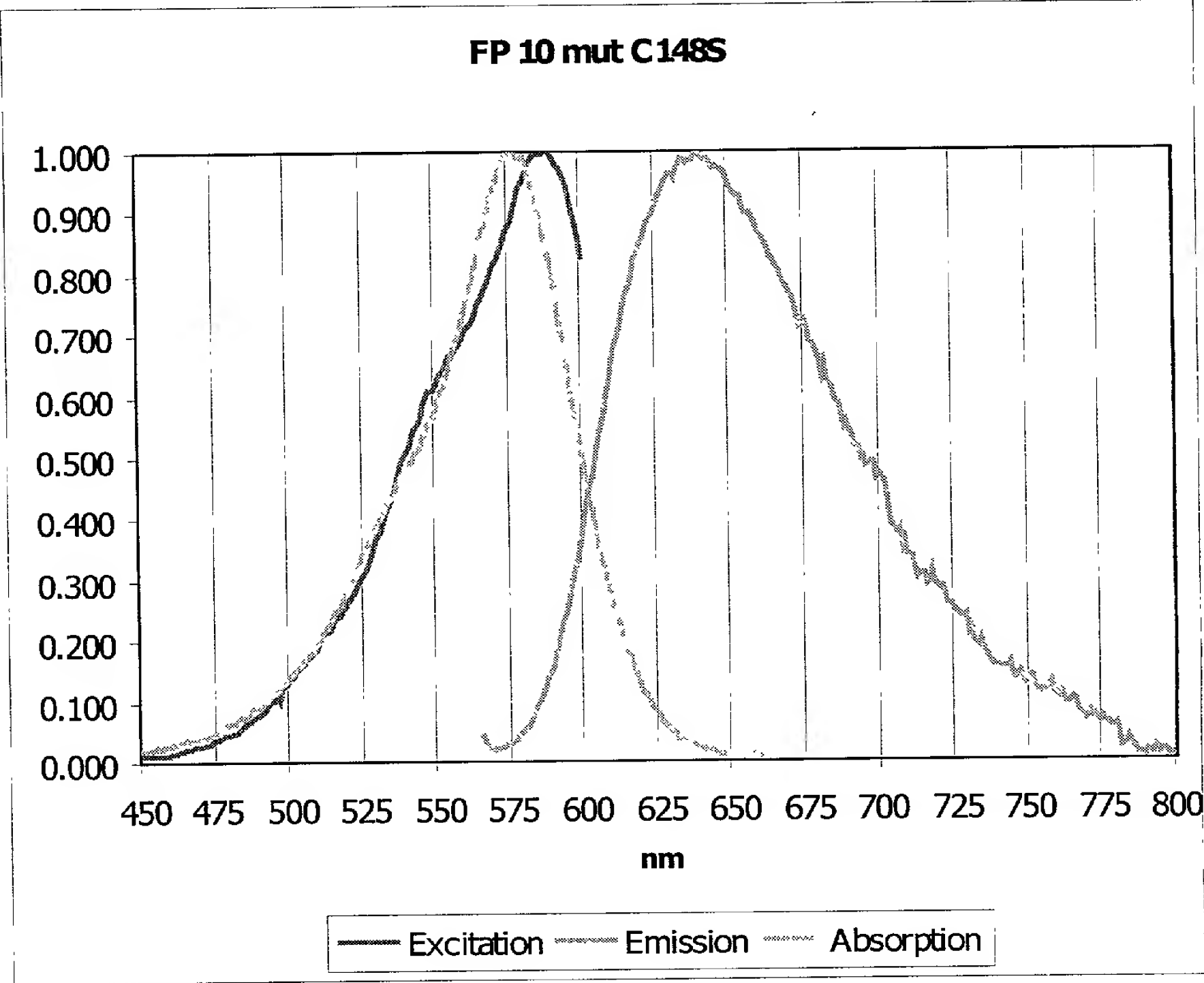


Figure 5B

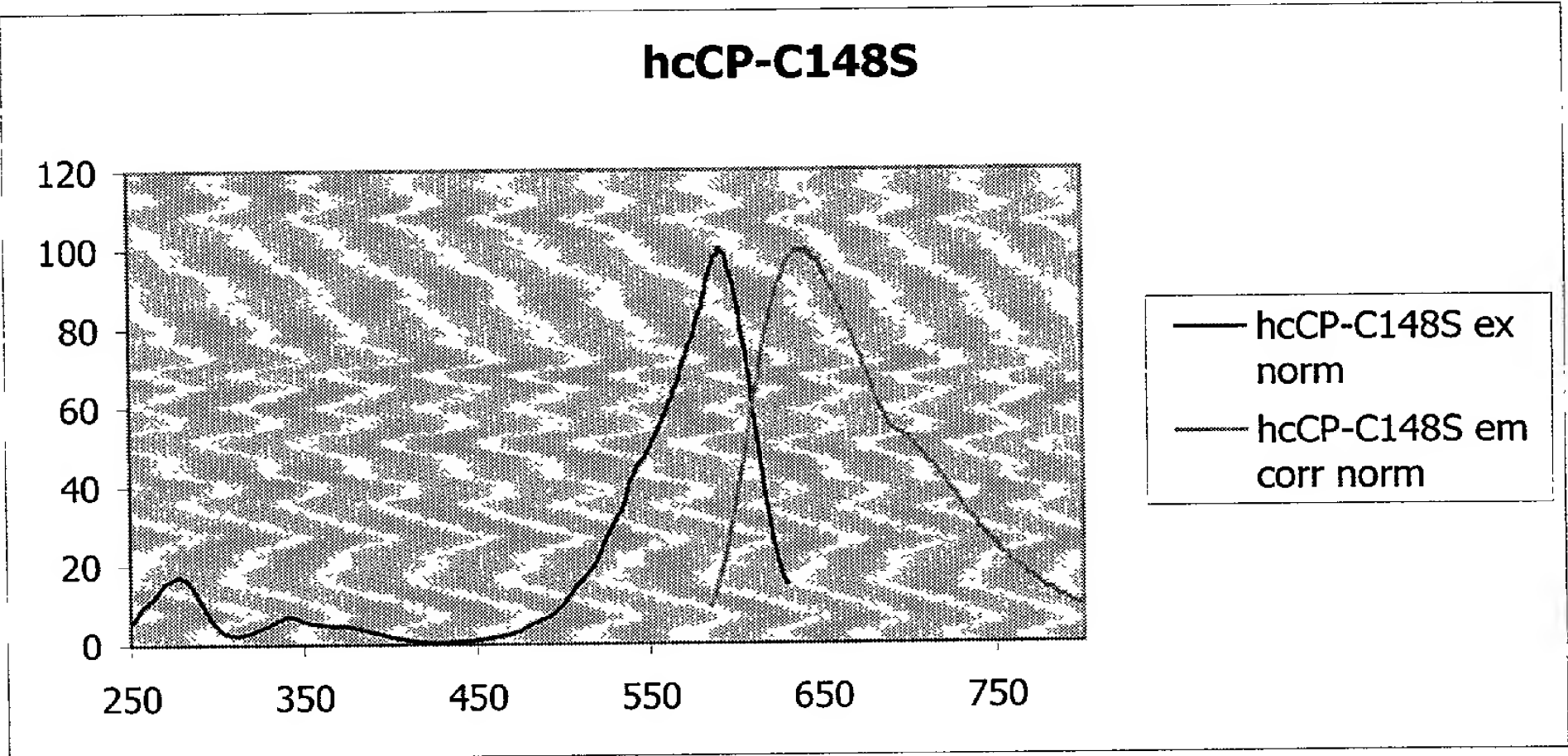


Figure 6

Heteractis crispa fluorescent protein mutant 44-9

point mutations: A5S,T39A,C148S,L181H,P208L,K211E according to GFP
numbering

A2S,T36A,C143S,L173H,P201L,K204E according to self-
numbering.

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      80      90      100      110      120
      TCTGGTTTGTGTTGAAAGAAAGTATGCGCATCAAGATGTACAT
      S G L L K E S M R I K M Y M

      130      140      150      160      170      180
GGAAGGCACGGTTAATGGCCATTATTTCAAGTGTGAAGGAGAGGGAGACGGCAACCCATT
E G T V N G H Y F K C E G E G D G N P F

      190      200      210      220      230      240
TGCAGGTACGCAGAGCATGAGGATTCATGTCACCGAAGGGGCTCCATTACCATTTCGCTT
A G T Q S M R I H V T E G A P L P F A F

      250      260      270      280      290      300
CGACATTTTGGCACCGTGTGTGAGTACGGCAGCAGGACCTTTGTCCACCATACGGCAGA
D I L A P C C E Y G S R T F V H H T A E

      310      320      330      340      350      360
GATTCCCGATTTCCTTCAAGCAGTCTTTCCTGAAGGCTTTACTTGGGAAAGAACCACAAC
I P D F F K Q S F P E G F T W E R T T T

      370      380      390      400      410      420
CTATGAAGATGGAGGCATTCTTACTGCTCATCAGGACACAAGCCTGGAGGGGAACTGCCT
Y E D G G I L T A H Q D T S L E G N C L

      430      440      450      460      470      480
TATATACAAGGTGAAAGTCCTTGGTACCAATTTTCCTGCTGATGGCCCCGTGATGAAGAA
I Y K V K V L G T N F P A D G P V M K N

      490      500      510      520      530      540
CAAATCAGGAGGATGGGAGCCAAGCACTGAGGTGGTTTATCCAGAGAATGGTGTCTCTGTG
K S G G W E P S T E V V Y P E N G V L C

      550      560      570      580      590      600
TGGACGTAATGTGATGGCCCTTAAAGTCGGTGATCGTCGTTTGATCTGCCATCACTATAC
G R N V M A L K V G D R R L I C H H Y T

      610      620      630      640      650      660
TTCTTACAGGTCCAAGAAAGCAGTCCGTGCCTTGACAATGCCAGGATTTTCATTTTACAGA
S Y R S K K A V R A L T M P G F H F T D

      670      680      690      700      710      720
CATCCGCCTTCAGATGCTGAGGAAAGAGAAAGACGAGTACTTTGAACTGTACGAAGCATC
I R L Q M L R K E K D E Y F E L Y E A S

      730      740      750      760
TGTGGCTAGGTACAGTGATCTTCCTGAAAAAGCAAATTGA
V A R Y S D L P E K A N * (SEQ ID NOs: 07 & 08)
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Figure 7A

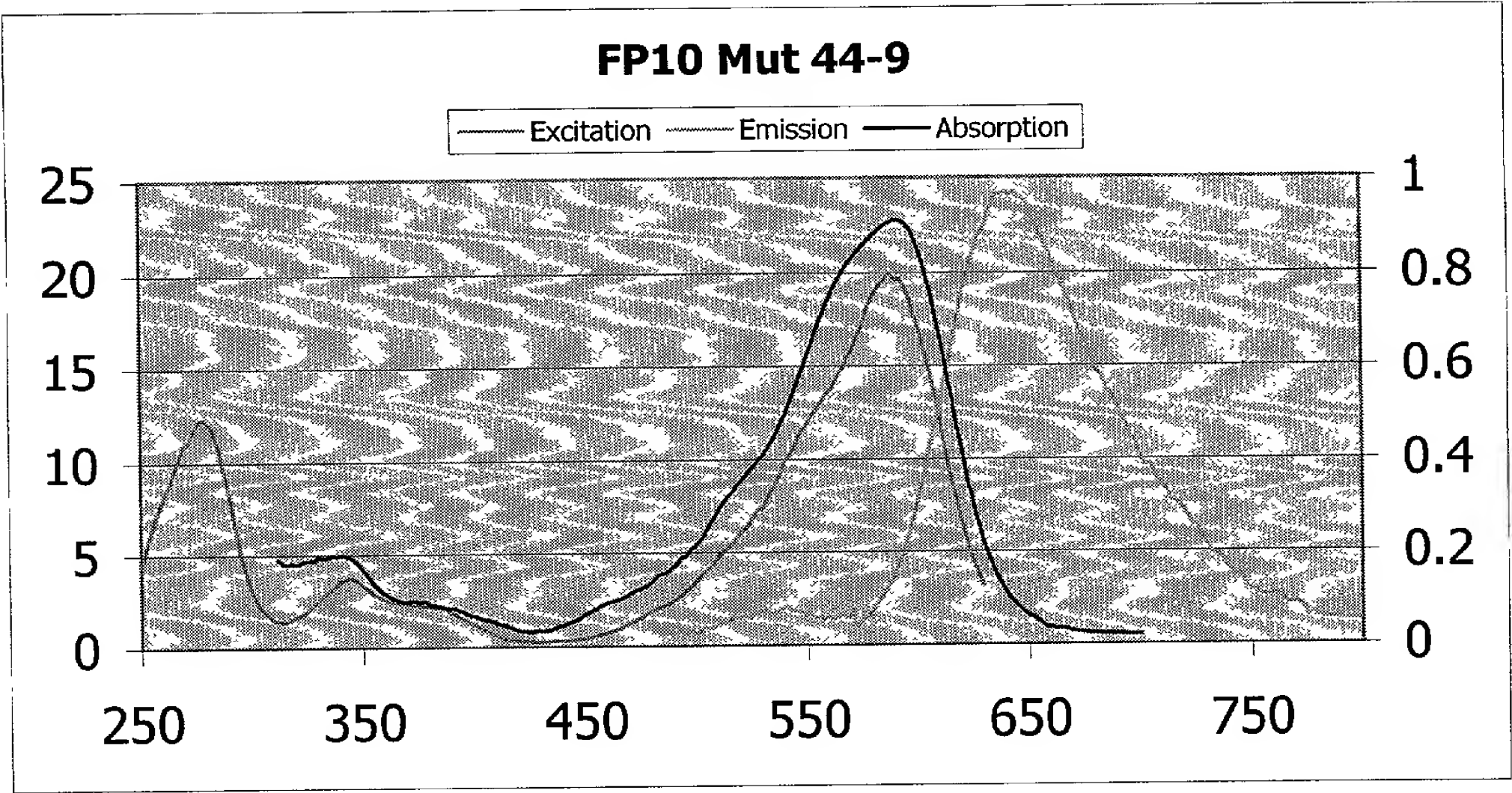


Figure 7B

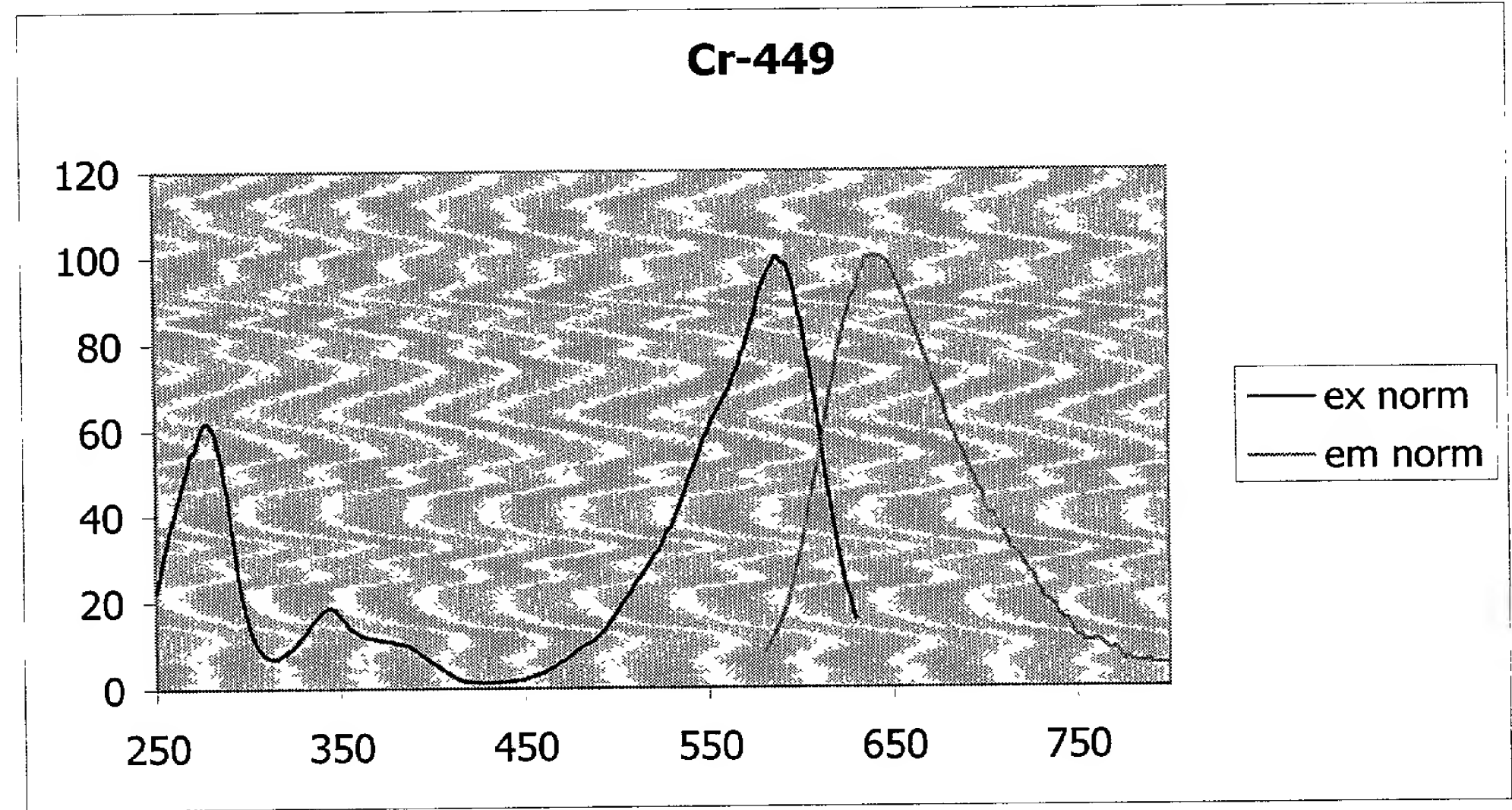


Figure 8

Crispa 44-6 mutant possesses six amino acid substitutions vs. wild type:
A2S,T36A,A65E,C143S,L173H,P201L.

TCTGGTTTGTGAAAGAAAGTATGCGCATCAAGATGTACAT
S G L L K E S M R I K M Y M

GGAAGGCACGGTTAATGGCCATTATTTCAAGTGTGAAGGAGAGGGAGACGGCAACCCATT
E G T V N G H Y F K C E G E G D G N P F

TGCAGGTACGCAGAGCATGAGGATTCATGTCACCGAAGGGGCTCCATTACCATTTCGCTT
A G T Q S M R I H V T E G A P L P F A F

CGACATTTTGGCACCGTGTGTGCGTACGGCAGCAGGACCTTTGTCCACCATAACGGCAGA
D I L A P C C A Y G S R T F V H H T A E

GATTCCCGATTTCTTCAAGCAGTCTTTCCTGAAGGCTTTACTTGGGAAAGAACCACAAC
I P D F F K Q S F P E G F T W E R T T T

CTATGAAGATGGAGGCATTCTTACTGCTCATCAGGACACAAGCCTGGAGGGGAACTGCCT
Y E D G G I L T A H Q D T S L E G N C L

←

TATATACAAGGTGAAAGTCCTTGGTACCAATTTTCCTGCTGATGGCCCCGTGATGAAGAA
I Y K V K V L G T N F P A D G P V M K N

CAAATCAGGAGGATGGGAGCCAAGCACTGAGGTGGTTTATCCAGAGAATGGTGTCTCTGTG
K S G G W E P S T E V V Y P E N G V L C

TGGACGTAATGTGATGGCCCTTAAAGTCGGTGATCGTCGTTTGATCTGCCATCACTATAC
G R N V M A L K V G D R R L I C H H Y T

TTCTTACAGGTCCAAGAAAGCAGTCCGTGCCTTGACAATGCCAGGATTTTATTTTACAGA
S Y R S K K A V R A L T M P G F H F T D

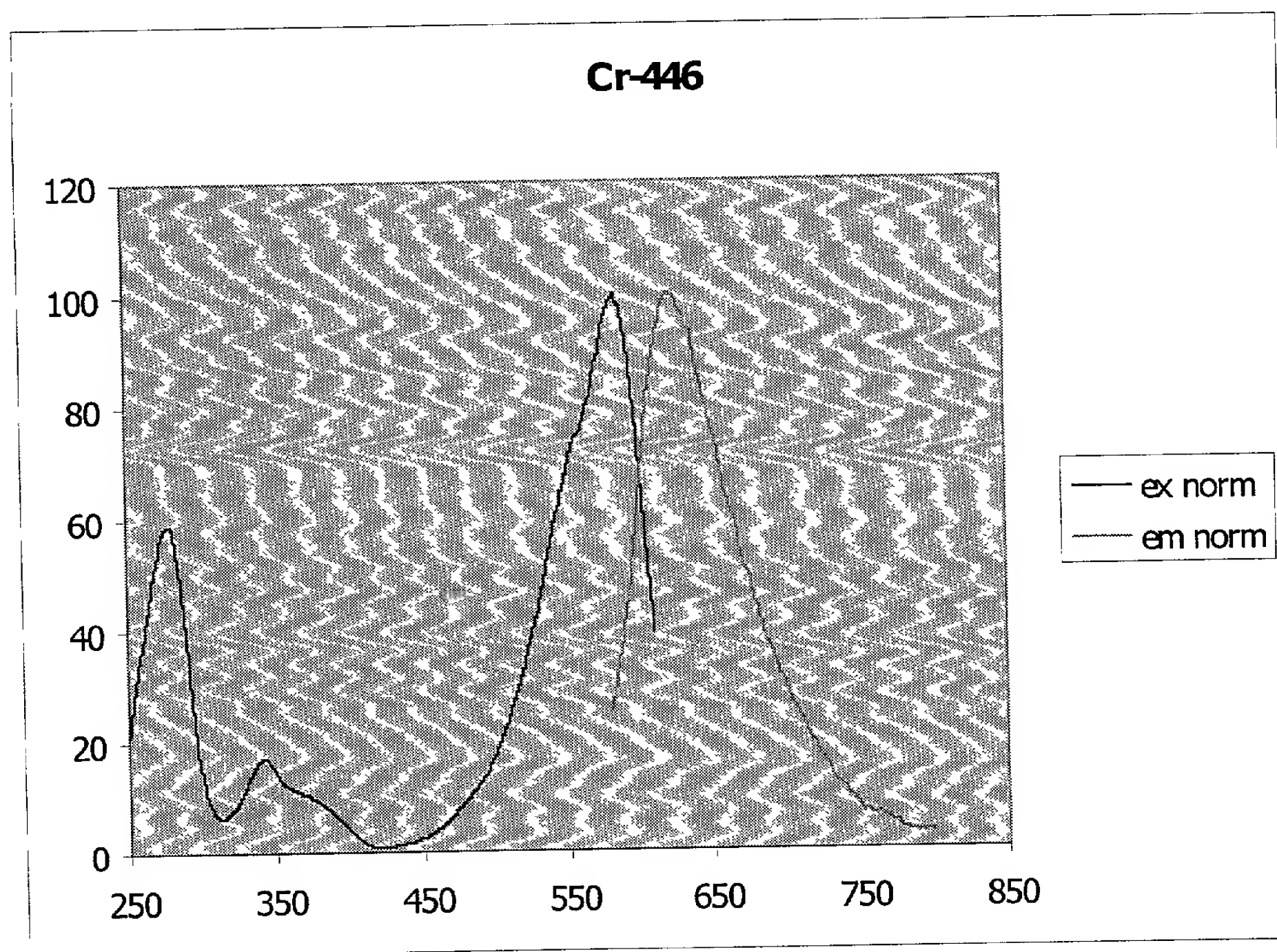
CATCCGCCTTCAGATGCTGAGGAAAGAGAAAGACGAGTACTTTGAACTGTACGAAGCATC
I R L Q M L R K E K D E Y F E L Y E A S

TGTGGCTAGGTACAGTGATCTTCCTGAAAAAGCAAATTGA
V A R Y S D L P E K A N *

(SEQ ID NO: 09 & 10)

0992692660

Figure 9



FOR FOT 6292650

Figure 10

The amino acid sequence of FP10-cr1 is:

M S G L L K E S M R I K M Y M E G T V N G H Y
F K C E G E G D G N P F A G T Q S M R I H V T
E G A P L P F A F D I L A P C C E Y G S R T F
V H H T A E I P D F F K Q S F P E G F T W E R
T T T Y E D G G I L T A H Q D T S L E G N C L
I Y K V K V H G T N F P A D G P V M K N K S G
G W E P S T E V V Y P E N G V L C G R N V M A
L K V G D R H L I C H H Y T S Y R S K K A V R
A L T M P G F H F T D I R L Q M L R K K K D E
Y F E L Y E A S V A R Y S D L P E K A N (SEQ ID
NO:12)

A "humanized" nt sequence encoding the above cr-1 mutant is:

ATGGTGAGCGGCCTGCTGAAGGAGAGTATGCGCATCAAGATGTACATGGAGGGCACC GTGAACGGCCAC
TACTTCAAGTGCGAGGGCGAGGGCGACGGCAACCCCTTCGCCGGCACCAGAGCATGAGAATCCACGTG
ACCGAGGGCGCCCCCTGCCCTTCGCCTTCGACATCCTGGCCCCCTGCTGCGAGTACGGCAGCAGGACC
TTCGTGCACCACACCGCCGAGATCCCCGACTTCTTCAAGCAGAGCTTCCCCGAGGGCTTCACCTGGGAG
AGAACCACCACCTACGAGGACGGCGGCATCCTGACCGCCCACCAGGACACCAGCCTGGAGGGCAACTGC
CTGATCTACAAGGTGAAGGTGCACGGCACCAACTTCCCCGCCGACGGCCCCGTGATGAAGAACAAGAGC
GGCGGCTGGGAGCCCAGCACCGAGGTGGTGTACCCCGAGAACGGCGTGCTGTGCGGCCGGAACGTGATG
GCCCTGAAGGTGGGCGACCGGCACCTGATCTGCCACCACTACACCAGCTACCGGAGCAAGAAGGCCGTG
CGCGCCCTGACCATGCCCCGGCTTCACTTCACCGACATCCGGCTCCAGATGCTGCGGAAGAAGAAGGAC
GAGTACTTCGAGCTGTACGAGGCCAGCGTGGCCCGGTACAGCGACCTGCCCGAGAAGGCCAACTGA
(SEQ ID NO:11)

Alternative cr1 amino acid sequence

MSGLLKESMRIKMYMEGTVNGHYFKCEGE GDNPFAGTQSMRIHVTEGAPLPFAFDILAPCCEYGSRTF
VHHTAEIPDFFKQSFPEGFTWERTTTYEDGGILTAHQDTSLEGNCLIIYKVKVHGTNFPADGPVMKNKSG
GWEPESTEVVYPENGVLCGRNVMALKVGDRLICHHYTSYRSKKA VRALTMPGFHFTDIRLQMLRKEKDE
YFELYEASVARYSDLPEKAN* SEQ ID NO:14)

Amino acid sequence encoding above alternative sequence:

ATGGTGAGCGGCCTGCTGAAGGAGAGCATGCGCATCAAGATGTACATGGAGGGCACC GTGAACGGCCAC
TACTTCAAGTGCGAGGGCGAGGGCGACGGCAACCCCTTCGCCGGCACCAGAGCATGCGGATCCACGTG
ACCGAGGGCGCCCCCTGCCCTTCGCCTTCGACATCCTGGCCCCCTGCTGCGAGTACGGCAGCAGGACC
TTCGTGCACCACACCGCCGAGATCCCCGACTTCTTCAAGCAGAGCTTCCCCGAGGGCTTCACCTGGGAG
AGAACCACCACCTACGAGGACGGCGGCATCCTGACCGCCCACCAGGACACCAGCCTGGAGGGCAACTGC
CTGATCTACAAGGTGAAGGTGCTGGGCACCAACTTCCCCGCCGACGGCCCCGTGATGAAGAACAAGAGC
GGCGGCTGGGAGCCCAGCACCGAGGTGGTGTACCCCGAGAACGGCGTGCTGTGCGGCCGGAACGTGATG
GCCCTGAAGGTGGGCGACCGGCAGCTGATCTGCCACCACTACACCAGCTACCGGAGCAAGAAGGCCGTG
CGGGCCCTGACCATGCCCCGGCTTCACTTCACCGACATCCGGCTGCAGATGCTGCGGAAGGAGAAGGAC
GAGTACTTCGAGCTGTACGAGGCCAGCGTGGCCCGGTACAGCGACCTGCCCGAGAAGGCCAACTGA
(SEQ ID NO:13)

Figure 11

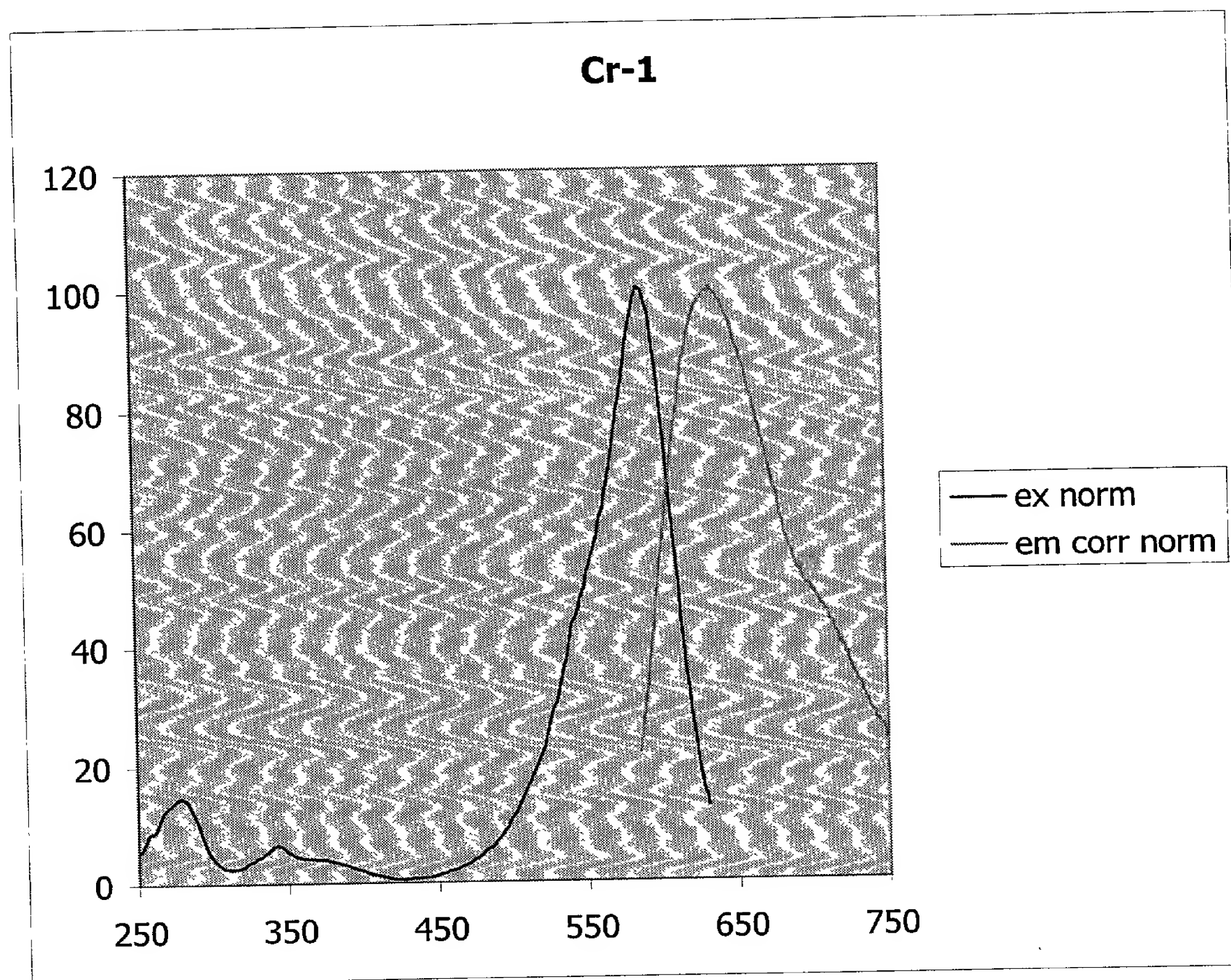


FIGURE 12

Cr-449-tandem (4-amino acid linker between monomers is in double underline).

| | | | | | | | | | | | | | | | | | |
|-----|-----|------------|------------|-----|-----|-----|-----|-----|-----|------------|------------|------------|------------|-----|-----|-----|-----|
| 1 | A | <u>CCG</u> | <u>GTC</u> | GCC | ACC | ATG | GTG | AGC | GGC | CTG | CTG | AAG | GAG | AGC | ATG | CGC | 46 |
| 1 | | AgeI | | | | M | V | S | G | L | L | K | E | S | M | R | 11 |
| 47 | ATC | AAG | ATG | TAC | ATG | GAG | GGC | ACC | GTG | AAC | GGC | CAC | TAC | TTC | AAG | TGC | 94 |
| 12 | I | K | M | Y | M | E | G | T | V | N | G | H | Y | F | K | C | 27 |
| 95 | GAG | GGC | GAG | GGC | GAC | GGC | AAC | CCC | TTC | GCC | GGC | ACC | CAG | AGC | ATG | CGG | 142 |
| 28 | E | G | E | G | D | G | N | P | F | A | G | T | Q | S | M | R | 43 |
| 143 | ATC | CAC | GTG | ACC | GAG | GGC | GCC | CCC | CTG | CCC | TTC | GCC | TTC | GAC | ATC | CTG | 190 |
| 44 | I | H | V | T | E | G | A | P | L | P | F | A | F | D | I | L | 59 |
| 191 | GCC | CCC | TGC | TGC | GAG | TAC | GGC | AGC | AGG | ACC | TTC | GTG | CAC | CAC | ACC | GCC | 238 |
| 60 | A | P | C | C | E | Y | G | S | R | T | F | V | H | H | T | A | 75 |
| 239 | GAG | ATC | CCC | GAC | TTC | TTC | AAG | CAG | AGC | TTC | CCC | GAG | GGC | TTC | ACC | TGG | 286 |
| 76 | E | I | P | D | F | F | K | Q | S | F | P | E | G | F | T | W | 91 |
| 287 | GAG | AGA | ACC | ACC | ACC | TAC | GAG | GAC | GGC | GGC | ATC | CTG | ACC | GCC | CAC | CAG | 334 |
| 92 | E | R | T | T | T | Y | E | D | G | G | I | L | T | A | H | Q | 107 |
| 335 | GAC | ACC | AGC | CTG | GAG | GGC | AAC | TGC | CTG | ATC | TAC | AAG | GTG | AAG | GTG | CTG | 382 |
| 108 | D | T | S | L | E | G | N | C | L | I | Y | K | V | K | V | L | 123 |
| 383 | GGC | ACC | AAC | TTC | CCC | GCC | GAC | GGC | CCC | GTG | ATG | AAG | AAC | AAG | AGC | GGC | 430 |
| 124 | G | T | N | F | P | A | D | G | P | V | M | K | N | K | S | G | 139 |
| 431 | GGC | TGG | GAG | CCC | AGC | ACC | GAG | GTG | GTG | TAC | CCC | GAG | AAC | GGC | GTG | CTG | 478 |
| 140 | G | W | E | P | S | T | E | V | V | Y | P | E | N | G | V | L | 155 |
| 479 | TGC | GGC | CGG | AAC | GTG | ATG | GCC | CTG | AAG | GTG | GGC | GAC | CGG | CGG | CTG | ATC | 526 |
| 156 | C | G | R | N | V | M | A | L | K | V | G | D | R | R | L | I | 171 |
| 527 | TGC | CAC | CAC | TAC | ACC | AGC | TAC | CGG | AGC | AAG | AAG | GCC | GTG | CGG | GCC | CTG | 574 |
| 172 | C | H | H | Y | T | S | Y | R | S | K | K | A | V | R | A | L | 187 |
| 575 | ACC | ATG | CCC | GGC | TTC | CAC | TTC | ACC | GAC | ATC | CGG | CTG | CAG | ATG | CTG | CGG | 622 |
| 188 | T | M | P | G | F | H | F | T | D | I | R | L | Q | M | L | R | 203 |
| 623 | AAG | GAG | AAG | GAC | GAG | TAC | TTC | GAG | CTG | TAC | GAG | GCC | AGC | GTG | GCC | CGG | 670 |
| 204 | K | E | K | D | E | Y | F | E | L | Y | E | A | S | V | A | R | 219 |
| 671 | TAC | AGC | GAC | CTG | CCC | GAG | AAG | GCC | AAC | <u>AGA</u> | <u>TCT</u> | <u>CCC</u> | <u>GGG</u> | ATG | GTG | AGC | 718 |
| 220 | Y | S | D | L | P | E | K | A | N | R | S | P | G | M | V | S | 235 |
| 719 | GGC | CTG | CTG | AAG | GAG | AGC | ATG | CGC | ATC | AAG | ATG | TAC | ATG | GAG | GGC | ACC | 766 |
| 236 | G | L | L | K | E | S | M | R | I | K | M | Y | M | E | G | T | 251 |
| 767 | GTG | AAC | GGC | CAC | TAC | TTC | AAG | TGC | GAG | GGC | GAG | GGC | GAC | GGC | AAC | CCC | 814 |
| 252 | V | N | G | H | Y | F | K | C | E | G | E | G | D | G | N | P | 267 |
| 815 | TTC | GCC | GGC | ACC | CAG | AGC | ATG | CGG | ATC | CAC | GTG | ACC | GAG | GGC | GCC | CCC | 862 |
| 268 | F | A | G | T | Q | S | M | R | I | H | V | T | E | G | A | P | 283 |
| 863 | CTG | CCC | TTC | GCC | TTC | GAC | ATC | CTG | GCC | CCC | TGC | TGC | GAG | TAC | GGC | AGC | 910 |
| 284 | L | P | F | A | F | D | I | L | A | P | C | C | E | Y | G | S | 299 |

0997673-10460

Figure 12 (continued)

| | | | | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| 911 | AGG | ACC | TTC | GTG | CAC | CAC | ACC | GCC | GAG | ATC | CCC | GAC | TTC | TTC | AAG | CAG | 958 |
| 300 | R | T | F | V | H | H | T | A | E | I | P | D | F | F | K | Q | 315 |
| | | | | | | | | | | | | | | | | | |
| 959 | AGC | TTC | CCC | GAG | GGC | TTC | ACC | TGG | GAG | AGA | ACC | ACC | ACC | TAC | GAG | GAC | 1006 |
| 316 | S | F | P | E | G | F | T | W | E | R | T | T | T | Y | E | D | 331 |
| | | | | | | | | | | | | | | | | | |
| 1007 | GGC | GGC | ATC | CTG | ACC | GCC | CAC | CAG | GAC | ACC | AGC | CTG | GAG | GGC | AAC | TGC | 1054 |
| 332 | G | G | I | L | T | A | H | Q | D | T | S | L | E | G | N | C | 347 |
| | | | | | | | | | | | | | | | | | |
| 1055 | CTG | ATC | TAC | AAG | GTG | AAG | GTG | CTG | GGC | ACC | AAC | TTC | CCC | GCC | GAC | GGC | 1102 |
| 348 | L | I | Y | K | V | K | V | L | G | T | N | F | P | A | D | G | 363 |
| | | | | | | | | | | | | | | | | | |
| 1103 | CCC | GTG | ATG | AAG | AAC | AAG | AGC | GGC | GGC | TGG | GAG | CCC | AGC | ACC | GAG | GTG | 1150 |
| 364 | P | V | M | K | N | K | S | G | G | W | E | P | S | T | E | V | 379 |
| | | | | | | | | | | | | | | | | | |
| 1151 | GTG | TAC | CCC | GAG | AAC | GGC | GTG | CTG | TGC | GGC | CGG | AAC | GTG | ATG | GCC | CTG | 1198 |
| 380 | V | Y | P | E | N | G | V | L | C | G | R | N | V | M | A | L | 395 |
| | | | | | | | | | | | | | | | | | |
| 1199 | AAG | GTG | GGC | GAC | CGG | CGG | CTG | ATC | TGC | CAC | CAC | TAC | ACC | AGC | TAC | CGG | 1246 |
| 396 | K | V | G | D | R | R | L | I | C | H | H | Y | T | S | Y | R | 411 |
| | | | | | | | | | | | | | | | | | |
| 1247 | AGC | AAG | AAG | GCC | GTG | CGG | GCC | CTG | ACC | ATG | CCC | GGC | TTC | CAC | TTC | ACC | 1294 |
| 412 | S | K | K | A | V | R | A | L | T | M | P | G | F | H | F | T | 427 |
| | | | | | | | | | | | | | | | | | |
| 1295 | GAC | ATC | CGG | CTG | CAG | ATG | CTG | CGG | AAG | GAG | AAG | GAC | GAG | TAC | TTC | GAG | 1342 |
| 428 | D | I | R | L | Q | M | L | R | K | E | K | D | E | Y | F | E | 443 |
| | | | | | | | | | | | | | | | | | |
| 1343 | CTG | TAC | GAG | GCC | AGC | GTG | GCC | CGG | TAC | AGC | GAC | CTG | CCC | GAG | AAG | GCC | 1390 |
| 444 | L | Y | E | A | S | V | A | R | Y | S | D | L | P | E | K | A | 459 |
| | | | | | | | | | | | | | | | | | |
| 1391 | AAC | TGA | | | | | | | | | | | | | | | |
| 460 | N | * | | | | | | | | | | | | | | | |

(SEQ ID NOS. 15 & 16)

FIG. 12 (continued)

Figure 13

Cr-449-tandem-actin (4-amino acid linker between Cr-449 monomers is noted in double underline; 4-amino acid linker between second Cr-449 and actin is noted in dashed underline).

| | | | | | | | | | | | | | | | | | |
|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|------------|------------|------------|------------|-----|-----|-----|-----|
| 1 | A | CCG | GTC | GCC | ACC | ATG | GTG | AGC | GGC | CTG | CTG | AAG | GAG | AGC | ATG | CGC | 46 |
| 1 | | AgeI | | | | M | V | S | G | L | L | K | E | S | M | R | 11 |
| 47 | ATC | AAG | ATG | TAC | ATG | GAG | GGC | ACC | GTG | AAC | GGC | CAC | TAC | TTC | AAG | TGC | 94 |
| 12 | I | K | M | Y | M | E | G | T | V | N | G | H | Y | F | K | C | 27 |
| 95 | GAG | GGC | GAG | GGC | GAC | GGC | AAC | CCC | TTC | GCC | GGC | ACC | CAG | AGC | ATG | CGG | 142 |
| 28 | E | G | E | G | D | G | N | P | F | A | G | T | Q | S | M | R | 43 |
| 143 | ATC | CAC | GTG | ACC | GAG | GGC | GCC | CCC | CTG | CCC | TTC | GCC | TTC | GAC | ATC | CTG | 190 |
| 44 | I | H | V | T | E | G | A | P | L | P | F | A | F | D | I | L | 59 |
| 191 | GCC | CCC | TGC | TGC | GAG | TAC | GGC | AGC | AGG | ACC | TTC | GTG | CAC | CAC | ACC | GCC | 238 |
| 60 | A | P | C | C | E | Y | G | S | R | T | F | V | H | H | T | A | 75 |
| 239 | GAG | ATC | CCC | GAC | TTC | TTC | AAG | CAG | AGC | TTC | CCC | GAG | GGC | TTC | ACC | TGG | 286 |
| 76 | E | I | P | D | F | F | K | Q | S | F | P | E | G | F | T | W | 91 |
| 287 | GAG | AGA | ACC | ACC | ACC | TAC | GAG | GAC | GGC | GGC | ATC | CTG | ACC | GCC | CAC | CAG | 334 |
| 92 | E | R | T | T | T | Y | E | D | G | G | I | L | T | A | H | Q | 107 |
| 335 | GAC | ACC | AGC | CTG | GAG | GGC | AAC | TGC | CTG | ATC | TAC | AAG | GTG | AAG | GTG | CTG | 382 |
| 108 | D | T | S | L | E | G | N | C | L | I | Y | K | V | K | V | L | 123 |
| 383 | GGC | ACC | AAC | TTC | CCC | GCC | GAC | GGC | CCC | GTG | ATG | AAG | AAC | AAG | AGC | GGC | 430 |
| 124 | G | T | N | F | P | A | D | G | P | V | M | K | N | K | S | G | 139 |
| 431 | GGC | TGG | GAG | CCC | AGC | ACC | GAG | GTG | GTG | TAC | CCC | GAG | AAC | GGC | GTG | CTG | 478 |
| 140 | G | W | E | P | S | T | E | V | V | Y | P | E | N | G | V | L | 155 |
| 479 | TGC | GGC | CGG | AAC | GTG | ATG | GCC | CTG | AAG | GTG | GGC | GAC | CGG | CGG | CTG | ATC | 526 |
| 156 | C | G | R | N | V | M | A | L | K | V | G | D | R | R | L | I | 171 |
| 527 | TGC | CAC | CAC | TAC | ACC | AGC | TAC | CGG | AGC | AAG | AAG | GCC | GTG | CGG | GCC | CTG | 574 |
| 172 | C | H | H | Y | T | S | Y | R | S | K | K | A | V | R | A | L | 187 |
| 575 | ACC | ATG | CCC | GGC | TTC | CAC | TTC | ACC | GAC | ATC | CGG | CTG | CAG | ATG | CTG | CGG | 622 |
| 188 | T | M | P | G | F | H | F | T | D | I | R | L | Q | M | L | R | 203 |
| 623 | AAG | GAG | AAG | GAC | GAG | TAC | TTC | GAG | CTG | TAC | GAG | GCC | AGC | GTG | GCC | CGG | 670 |
| 204 | K | E | K | D | E | Y | F | E | L | Y | E | A | S | V | A | R | 219 |
| 671 | TAC | AGC | GAC | CTG | CCC | GAG | AAG | GCC | AAC | <u>AGA</u> | <u>TCT</u> | <u>CCC</u> | <u>GGG</u> | ATG | GTG | AGC | 718 |
| 220 | Y | S | D | L | P | E | K | A | N | R | S | P | G | M | V | S | 235 |
| 719 | GGC | CTG | CTG | AAG | GAG | AGC | ATG | CGC | ATC | AAG | ATG | TAC | ATG | GAG | GGC | ACC | 766 |
| 236 | G | L | L | K | E | S | M | R | I | K | M | Y | M | E | G | T | 251 |
| 767 | GTG | AAC | GGC | CAC | TAC | TTC | AAG | TGC | GAG | GGC | GAG | GGC | GAC | GGC | AAC | CCC | 814 |
| 252 | V | N | G | H | Y | F | K | C | E | G | E | G | D | G | N | P | 267 |
| 815 | TTC | GCC | GGC | ACC | CAG | AGC | ATG | CGG | ATC | CAC | GTG | ACC | GAG | GGC | GCC | CCC | 862 |
| 268 | F | A | G | T | Q | S | M | R | I | H | V | T | E | G | A | P | 283 |

09694660
T02T0E2994660

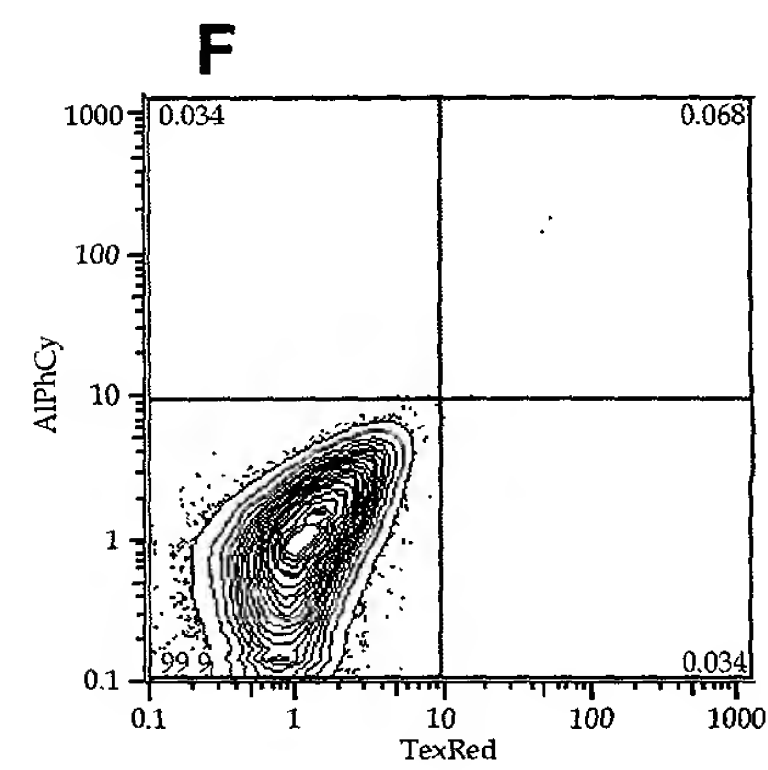
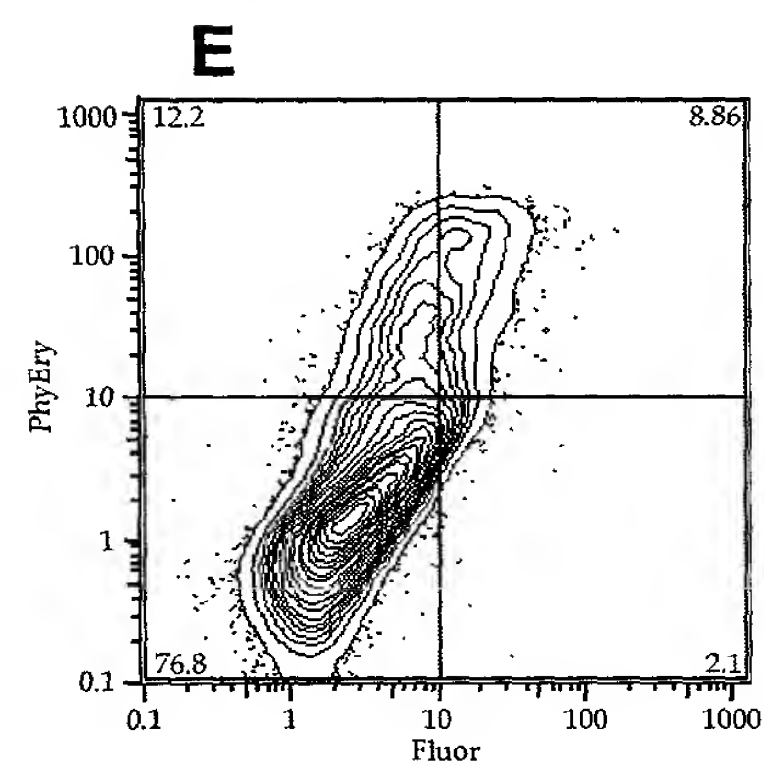
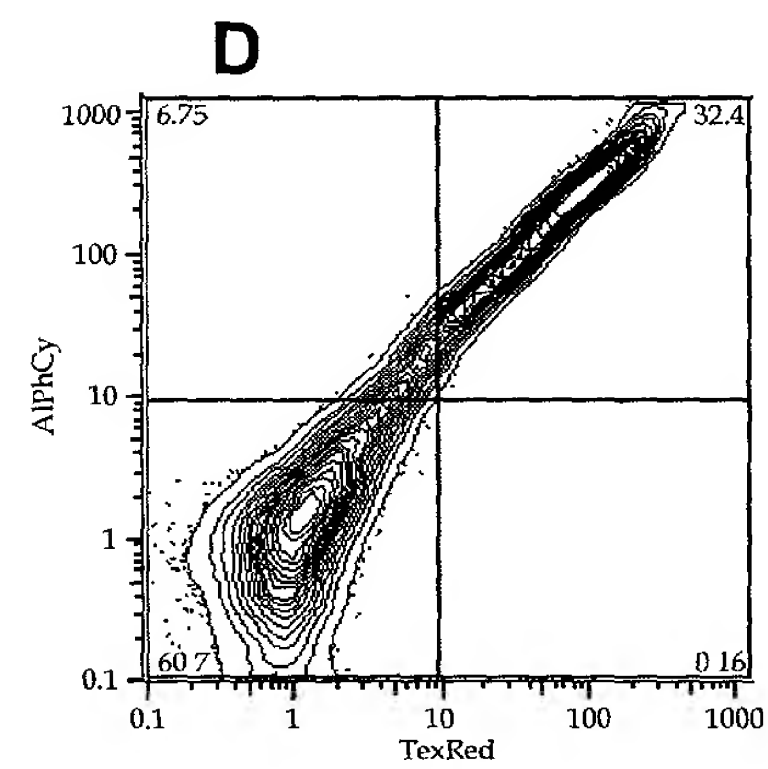
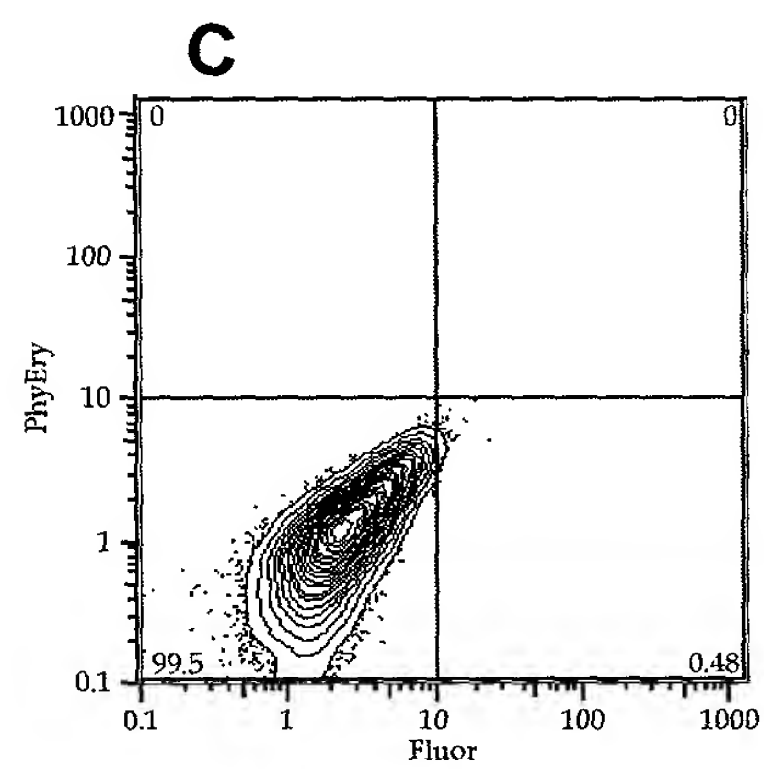
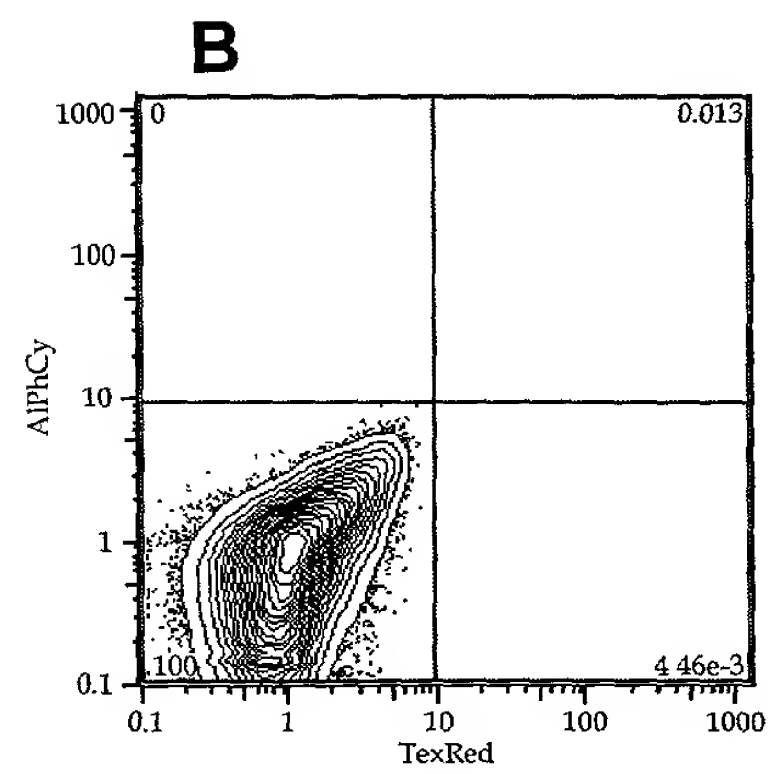
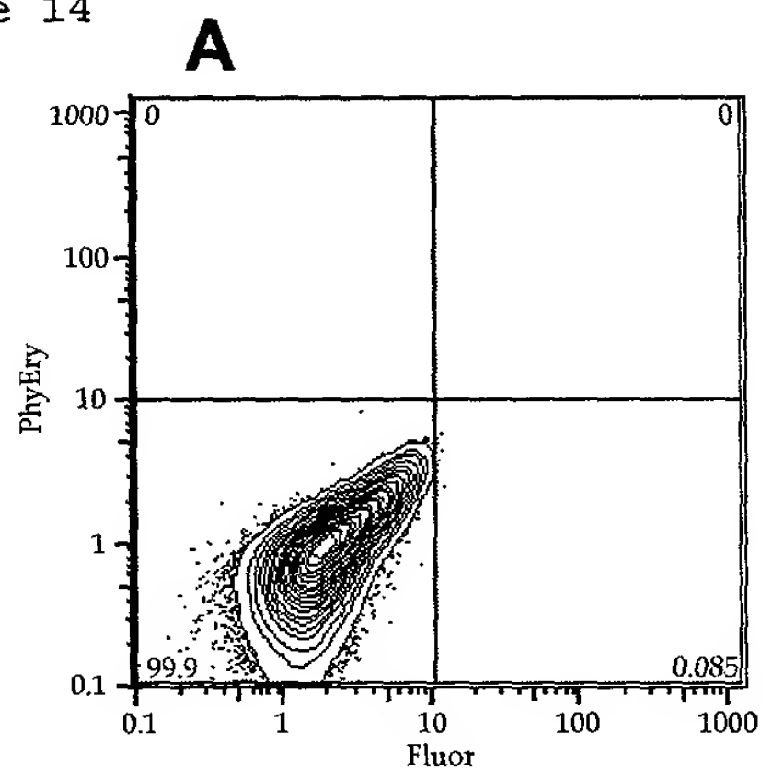
Figure 13 (continued)

| | | | | | | | | | | | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|-----|-----|-----|-----|------|
| 863 | CTG | CCC | TTC | GCC | TTC | GAC | ATC | CTG | GCC | CCC | TGC | TGC | GAG | TAC | GGC | AGC | 910 |
| 284 | L | P | F | A | F | D | I | L | A | P | C | C | E | Y | G | S | 299 |
| 911 | AGG | ACC | TTC | GTG | CAC | CAC | ACC | GCC | GAG | ATC | CCC | GAC | TTC | TTC | AAG | CAG | 958 |
| 300 | R | T | F | V | H | H | T | A | E | I | P | D | F | F | K | Q | 315 |
| 959 | AGC | TTC | CCC | GAG | GGC | TTC | ACC | TGG | GAG | AGA | ACC | ACC | ACC | TAC | GAG | GAC | 1006 |
| 316 | S | F | P | E | G | F | T | W | E | R | T | T | T | Y | E | D | 331 |
| 1007 | GGC | GGC | ATC | CTG | ACC | GCC | CAC | CAG | GAC | ACC | AGC | CTG | GAG | GGC | AAC | TGC | 1054 |
| 332 | G | G | I | L | T | A | H | Q | D | T | S | L | E | G | N | C | 347 |
| 1055 | CTG | ATC | TAC | AAG | GTG | AAG | GTG | CTG | GGC | ACC | AAC | TTC | CCC | GCC | GAC | GGC | 1102 |
| 348 | L | I | Y | K | V | K | V | L | G | T | N | F | P | A | D | G | 363 |
| 1103 | CCC | GTG | ATG | AAG | AAC | AAG | AGC | GGC | GGC | TGG | GAG | CCC | AGC | ACC | GAG | GTG | 1150 |
| 364 | P | V | M | K | N | K | S | G | G | W | E | P | S | T | E | V | 379 |
| 1151 | GTG | TAC | CCC | GAG | AAC | GGC | GTG | CTG | TGC | GGC | CGG | AAC | GTG | ATG | GCC | CTG | 1198 |
| 380 | V | Y | P | E | N | G | V | L | C | G | R | N | V | M | A | L | 395 |
| 1199 | AAG | GTG | GGC | GAC | CGG | CGG | CTG | ATC | TGC | CAC | CAC | TAC | ACC | AGC | TAC | CGG | 1246 |
| 396 | K | V | G | D | R | R | L | I | C | H | H | Y | T | S | Y | R | 411 |
| 1247 | AGC | AAG | AAG | GCC | GTG | CGG | GCC | CTG | ACC | ATG | CCC | GGC | TTC | CAC | TTC | ACC | 1294 |
| 412 | S | K | K | A | V | R | A | L | T | M | P | G | F | H | F | T | 427 |
| 1295 | GAC | ATC | CGG | CTG | CAG | ATG | CTG | CGG | AAG | GAG | AAG | GAC | GAG | TAC | TTC | GAG | 1342 |
| 428 | D | I | R | L | Q | M | L | R | K | E | K | D | E | Y | F | E | 443 |
| 1343 | CTG | TAC | GAG | GCC | AGC | GTG | GCC | CGG | TAC | AGC | GAC | CTG | CCC | GAG | AAG | GCC | 1390 |
| 444 | L | Y | E | A | S | V | A | R | Y | S | D | L | P | E | K | A | 459 |
| 1391 | AAC | AGA | ACT | CGA | GCT | ATG | GAT | GAT | GAT | ATC | GCC | G... | | | | | 1424 |
| 460 | N | R | T | R | A | M | D | D | D | I | A... | | | | | | 470 |

actin

(SEQ ID NOS. 17 & 18).

Figure 14



FOOT E499660

Figure 15

Heteractis crispa chromoprotein hcCP mut C148S

C148S according to GFP numbering

C143S according to self-numbering.

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ATGGCTGGTTTGTGAAAGAAAGTATGCGCATCAAGATGTACAT
M A G L L K E S M R I K M Y M

GGAAGGCACGGTTAATGGCCATTATTTCAAGTGTGAAGGAGAGGGAGACGGCAACCCATT
E G T V N G H Y F K C E G E G D G N P F

TACAGGTACGCAGAGCATGAGGATTCATGTCACCGAAGGGGCTCCATTACCATTTCCTT
T G T Q S M R I H V T E G A P L P F A F

CGACATTTTGGCACCGTGTGTGAGTACGGCAGCAGGACCTTTGTCCACCATAACGGCAGA
D I L A P C C E Y G S R T F V H H T A E

GATTCCCGATTTCTTCAAGCAGTCTTTCCTGAAGGCTTTACTTGGGAAAGAACCACAAC
I P D F F K Q S F P E G F T W E R T T T

CTATGAAGATGGAGGCATTCTTACTGCTCATCAGGACACAAGCCTGGAGGGGAAGTGCCT
Y E D G G I L T A H Q D T S L E G N C L

TATATACAAGGTGAAAGTCCTTGGTACCAATTTTCCTGCTGATGGCCCCGTGATGAAGAA
I Y K V K V L G T N F P A D G P V M K N

CAAATCAGGAGGATGGGAGCCAAGCACTGAGGTGGTTTATCCAGAGAATGGTGTCCTGTG
K S G G W E P S T E V V Y P E N G V L C

TGGACGTAATGTGATGGCCCTTAAAGTCGGTGATCGTCGTTTGATCTGCCATCTCTATAC
G R N V M A L K V G D R R L I C H L Y T

TTCTTACAGGTCCAAGAAAGCAGTCCGTGCCTTGACAATGCCAGGATTTTCATTTTACAGA
S Y R S K K A V R A L T M P G F H F T D

CATCCGCCTTCAGATGCCGAGGAAAAAGAAAGACGAGTACTTTGAACTGTACGAAGCATC
I R L Q M P R K K K D E Y F E L Y E A S

TGTGGCTAGGTACAGTGATCTTCCTGAAAAAGCAAATTGA
V A R Y S D L P E K A N *
SEQ ID NO:23 & 24
```

0997693:101204

Figure 16

Crispa 44-6 mutant possesses six amino acid substitutions vs. wild type:
A2S,T36A,A65E,C143S,L173H,P201L.

TCTGGTTTGTGAAAGAAAGTATGCGCATCAAGATGTACAT
S G L L K E S M R I K M Y M

GGAAGGCACGGTTAATGGCCATTATTTCAAGTGTGAAGGAGAGGGAGACGGCAACCCATT
E G T V N G H Y F K C E G E G D G N P F

TGCAGGTACGCAGAGCATGAGGATTCATGTCACCGAAGGGGCTCCATTACCATTTCCTT
A G T Q S M R I H V T E G A P L P F A F

CGACATTTTGGCACCGTGTGTGCGTACGGCAGCAGGACCTTTGTCCACCATACGGCAGA
D I L A P C C A Y G S R T F V H H T A E

GATTCCCGATTTCTTCAAGCAGTCTTTCCTGAAGGCTTTACTTGGGAAAGAACCACAAC
I P D F F K Q S F P E G F T W E R T T T

CTATGAAGATGGAGGCATTCTTACTGCTCATCAGGACACAAGCCTGGAGGGGAACTGCCT
Y E D G G I L T A H Q D T S L E G N C L

←

TATATAAAGGTGAAAGTCCTTGGTACCAATTTTCCTGCTGATGGCCCCGTGATGAAGAA
I Y K V K V L G T N F P A D G P V M K N

CAAATCAGGAGGATGGGAGCCAAGCACTGAGGTGGTTTATCCAGAGAATGGTGTCTGTG
K S G G W E P S T E V V Y P E N G V L C

TGGACGTAATGTGATGGCCCTTAAAGTCGGTGATCGTCGTTTGATCTGCCATCACTATAC
G R N V M A L K V G D R R L I C H H Y T

TTCTTACAGGTCCAAGAAAGCAGTCCGTGCCTTGACAATGCCAGGATTTTATTTTACAGA
S Y R S K K A V R A L T M P G F H F T D

CATCCGCCTTCAGATGCTGAGGAAAAAGAAAGACGAGTACTTTGAACTGTACGAAGCATC
I R L Q M L R K K K D E Y F E L Y E A S

TGTGGCTAGGTACAGTGATCTTCCTGAAAAAGCAAATTGA
V A R Y S D L P E K A N *

SEQ ID NO:25 & 26

092667-10201
T02101-10201

Figure 17

Heteractis crispa chromoprotein wild type (base isoform)

10 20 30 40 50 60
 5' ACCATTTGCTTTGGTTCCTTGGCAAACGAAAGTTTAGAACGAAACTGACCCAAATTACA
 70 80 90 100 110 120
 TCTTCCTCCTGGATCCTTACCATGGCTGGTTTGGTTGAAAGAAAGTATGCGCATCAAGATG
 M A G L L K E S M R I K M
 130 140 150 160 170 180
 TACATGGAAGGCACGGTTAATGGCCATTATTTCAAGTGTGAAGGAGAGGGAGACGGCAAC
 Y M E G T V N G H Y F K C E G E G D G N
 190 200 210 220 230 240
 CCATTTACAGGTACGCAGAGCATGAGGATTCATGTCACCGAAGGGGCTCCATTACCATTT
 P F T G T Q S M R I H V T E G A P L P F
 250 260 270 280 290 300
 GCCTTCGACATTTTGGCACCGTGTGTGAGTACGGCAGCAGGACCTTTGTCCACCATACG
 A F D I L A P C C E Y G S R T F V H H T
 310 320 330 340 350 360
 GCAGAGATTCCCGATTTCTTCAAGCAGTCTTTCCTGAAGGCTTTACTTGGGAAAGAACC
 A E I P D F F K Q S F P E G F T W E R T
 370 380 390 400 410 420
 ACAACCTATGAAGATGGAGGCATTCTTACTGCTCATCAGGACACAAGCCTGGAGGGGAAC
 T T Y E D G G I L T A H Q D T S L E G N
 430 440 450 460 470 480
 TGCCTTATATACAAGGTGAAAGTCCTTGGTACCAATTTTCCTGCTGATGGCCCCGTGATG
 C L I Y K V K V L G T N F P A D G P V M
 490 500 510 520 530 540
 AAGAACAAATCAGGAGGATGGGAGCCATGCACTGAGGTGGTTTATCCAGAGAATGGTGTC
 K N K S G G W E P C T E V V Y P E N G V
 550 560 570 580 590 600
 CTGTGTGGACGTAATGTGATGGCCCTTAAAGTCGGTGATCGTCGTTTGATCTGCCATCTC
 L C G R N V M A L K V G D R R L I C H L
 610 620 630 640 650 660
 TATACTTCTTACAGGTCCAAGAAAGCAGTCCGTGCCTTGACAATGCCAGGATTTTCATTTT
 Y T S Y R S K K A V R A L T M P G F H F
 670 680 690 700 710 720
 ACAGACATCCGCCTTCAGATGCCGAGGAAAACGAAAGACGAGTACTTTGAACTGTACGAA
 T D I R L Q M P R K T K D E Y F E L Y E
 730 740 750 760 770 780
 GCATCTGTGGCTAGGTACAGTGATCTTCCTGAAAAAGCAAATTGATTGTTCCAGTGACA
 A S V A R Y S D L P E K A N *
 790 800 810 820 830 840
 CCAGACTGCTGTCAGCTTTTGGTTAAAGCCCGAAAGACAAAAGGACATTTGTAGTTTAGT
 850 860 870 880 890 900
 TTATATTTCCCTTTTCATTTGTGAATCAACATTGTACTCTCTGTAAACCTTTAAAATGCTC
 910
 CATTAAACCT 3' (SEQ ID NOs: 27 & 28)

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